

REMARKS

Applicant respectfully requests reconsideration. Claims 87-117 were previously pending in this application. Claim 87 has been amended to clarify that the at least two individual lipids are purified phospholipids. Support for the amendment can be found in the specification as filed at least throughout the examples section, at page 22 of the specification, and in claim 4 as originally filed. New claims 118 and 119 have been added. Support for claim 118 can be found in the specification as filed at least in currently pending claims 89, 90, 92, 93, 100, 102, 104, 107, 111-113, 115, and 117. Support for new claim 119 can be found at least in claim 99 as currently pending. As a result, claims 87-119 are pending for examination with claim 87 being an independent claim. No new matter has been added.

Rejections Under 35 U.S.C. §103

The Examiner rejected claims 87-111 and 117 under 35 U.S.C. §103(a) as being unpatentable over Nyberg (5,677,472) in view of Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination. Applicant respectfully traverses the rejection.

The Examiner states at page 2 of the Office Action “In view of Applicant’s arguments, Unger (6,521,211) is removed from the rejections.” The Examiner states at page 3 of the Office Action mailed August 13, 2009, that “Nyberg et al. and Unger teach steps a, b, and c” of the instant claim 87. Applicant respectfully requests clarification of the inclusion of the Unger reference in the body of the rejection.

With respect to issues raised in the remainder of the rejection, Applicant has amended claim 87 to clarify that the process as claimed includes contacting at least two separate, individual lipids with a first non-aqueous solvent that causes the lipids to dissolve and form a lipid solution. The contacting of the phospholipids with the non-aqueous solvent may include mixing separate phospholipids together and then contacting with the first non-aqueous solvent or may include adding separate phospholipids sequentially to the first non-aqueous solvent.

The Examiner concludes at page 2 of the Office Action that Nyberg et al. teaches steps a, b, and c of claim 87. Applicant respectfully disagrees. The steps of claim 87 include

contacting at least two purified phospholipids with a first non-aqueous solution to dissolve the phospholipids into a blended solution. The contact can be either adding each of the at least two phospholipids sequentially to the first non-aqueous solvent, or mixing the at least two phospholipids together and then adding the mixture to the first non-aqueous solvent to make a blended solution. The additional steps include contacting the blended solution with a second non-aqueous solution to precipitate the blended phospholipids, contacting the blended phospholipids with a third non-aqueous solvent to dissolve the phospholipids into a lipid blend solution, and contacting the lipid blend solution with an aqueous solution to yield a lipid suspension. Each step is important to permit preparation of the uniform phospholipid blend of the claimed invention, which reduces difficulties encountered with using alternative methods. Past difficulties have included lack of uniformity, lack of purity, difficulty in recovery of solids, etc. (see page 2 of specification as filed.)

The Examiner states at page 2:

Nyberg et al. disclose methods of preparing phospholipids precipitates comprising mixing a phospholipids blend containing phosphatidylcholine, phosphatidylethanolamine, and sphingomyelin in an organic solvent mixture of polar organic solvent (e.g. methanol and essential non-polar organic solvent (e.g. toluene), concentrating the solution, then add a second organic solvent of intermediate polarity (e.g. acetone and heptane) to cause precipitation of phospholipids at about 13°C-25°C, and drying the precipitate (see example 1, 2, 6, and claim 1).

As indicated by the Examiner in this quote, Nyberg starts with a mixture of phospholipids that is mixed with an organic solvent mixture to precipitate out the phospholipids. Nyberg does not teach or suggest starting with individual, separate, purified, phospholipids and does not teach adding each of the individual phospholipids sequentially to a first non-aqueous solvent or mixing each of the individual phospholipids together and then adding them to a non-aqueous solvent. The claims as amended are drawn to preparing a blend of at least two individual phospholipids and contacting the blend with a series of solvents to permit preparation of a uniform blend of phospholipids followed by use of that uniform blend to prepare a lipid suspension. Each step in claim 87, as amended, is important for the outcome of the process.

The Examiner states at page 4 of the Office Action that Nyberg's starting mixture contains "three individual phospholipids." Applicant submits that it is erroneous to interpret a "mixture" of lipids to mean three individual lipids. As described above, the at least two individual lipids in the claimed invention are separate lipids that are mixed together as part of the preparation process, a step that is clearly different than, and not taught or suggested by, Nyberg et al. Applicant submits that Nyberg does not teach any individual phospholipids, but clearly begins with a combination of phospholipids with the stated goal of separating out the phospholipids. One of ordinary skill in the art would not use the methods of Nyberg's separation to make the claimed invention when the claimed invention encompasses the opposite process, that of making a uniform blend of two or more previously separate phospholipids.

The amendment of claim 87 further clarifies that the phospholipids of the instant claims are separate, individual purified phospholipids that are combined in a step of the claimed process. In contrast, Nyberg et al. teaches separating out lipids from naturally occurring mixtures. Nyberg teaches a starting material that is a "phospholipids blend" that is exposed to solutions to separate out the phospholipids from the mixture for further use. Nyberg et al. fails to teach or suggest mixing together individual, separate phospholipids to make a lipid blend and therefore, at a minimum, fails to teach step (a), an element of claim 87.

The rejection does not suggest that the secondary references, Kissel et al., Kikuchi et al., Papahadjopoulos et al., or Lenk et al., teach any of steps a to c as claimed. The Examiner instead relies on these references as suggestive of steps d and e, as demonstrating that dissolving a solid lipid in a non-aqueous then aqueous solvent had been taught for the preparation of liposomes.

Kissel et al. describes preparing liposomes by dissolving lecithin in methylene chloride and adding an aqueous solution. Kissel et al. does not teach or suggest combining at least two phospholipids and contacting the phospholipid mixture with three non-aqueous solutions followed by an aqueous solution as set forth in claim 87, as amended. Similarly, Papahadjopoulos et al. describes methods of making liposomes by dissolving phospholipids in diethyl ether and adding an aqueous solution, and does not teach or suggest preparing a lipid suspension as in claim 87, as amended. Lenk et al. and Kikuchi et al. both describe dissolving phospholipids in an organic solvent followed by addition of an aqueous medium, and neither

reference teaches or suggests the instantly claimed process of using multiple steps of contacting with multiple non-aqueous solvents to prepare a uniform lipid blend after combining at least two individual lipids in a manner as claimed.

The Examiner bases the rejection, in part, on his conclusion that one skilled in the art would add the two additional steps of dissolving previously separate phospholipids in three different non-aqueous solvents to make a lipid blend. None of the cited references, either alone or in combination, teaches or suggests these steps. Therefore, the combination of references fails to provide a basis for the obviousness rejection because each element of the invention as claimed is not taught or suggested by the combination and also, because there is no “apparent reason to combine the known elements in the fashion claimed.” *KSR Int'l Co. v. Teleflex, Inc.*, 550; 421 U.S. 398 (2007). The Examiner’s conclusion of obviousness appears to be based on the impermissible application of hindsight reasoning. A *prima facie* case for obviousness has not been made.

The combination of the teaching of the primary reference, Nyberg et al., with any one or a combination of Kissel et al., Kikuchi et al., Papahadjopoulos et al., and Lenk et al. fails to teach each element of the invention as claimed and the combination of the teaching does not result in the claimed invention. The combination of references fails to support a *prima facie* case of obviousness. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 87-111, and 117 under 35 U.S.C. §103(a), as unpatentable over Nyberg et al. in view of Kissel et al., Papahadjopoulos et al., Lenk et al., and Kikuchi et al., individually or in combination.

The Examiner rejected claims 111-114 under 35 U.S.C. §103(a) as being unpatentable over Nyberg (5,677,472) in view of Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination, further in view of Swaerd-Nordmo (6,165,442). Applicant respectfully traverses the rejection.

Rejected claims 111-114 ultimately depend from claim 87. As discussed above, Applicant submits that all elements of claim 87, as amended, are not taught or suggested by the combination of Nyberg et al., in view of Kissel et al., Kikuchi et al., Papahadjopoulos et al., and

Lenk et al. The addition of the teaching of Swaerd-Nordmo et al. to the combination does not remedy the deficit.

The Examiner states at page 6 of the Office Action, that the Swaerd-Nordmo reference “is combined for its teaching of encapsulating ultrasound contrast agents; Nyberg et al. teaches the preparation of phospholipids using instant steps a to c.” As set forth above, Nyberg et al. teaches the separation of combined lipids and fails to teach or suggest any process that includes steps a to c of the invention as claimed, which result in a uniform blend of phospholipids. The combination of the teaching of Kissel et al., Kikuchi et al., Papahadjopoulos et al., or Lenk et al. with that of Nyberg et al., fails to remedy the omission. The addition of the teaching of Swaerd-Nordmo et al. to the combination of the references also fails to teach or suggest each element of the claimed invention and a *prima facie* case for obviousness has not been established.

Accordingly, Applicant requests reconsideration and withdrawal of the rejection of claims 111-114 under 35 U.S.C. §103(a) as unpatentable over Nyberg in view of Kissel or Papahadjopoulos or Lenk or Kikuchi, individually or in combination, further in view of Swaerd-Nordmo.

The Examiner rejected claims 115-116 under 35 U.S.C. §103(a) as being unpatentable over Nyberg (5,677,472) in view of Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination, further in view of Swaerd-Nordmo, further in view of Unger (6,071,495). Applicant respectfully traverses the rejection.

Rejected claims 115-116 depend from claim 112, and ultimately depend from claim 87. As discussed above, all elements of claim 87, as amended, are not taught or suggested by the combination of Nyberg et al., in view of Kissel et al., Kikuchi et al., Papahadjopoulos et al., and Lenk et al. in view of Swaerd-Nordmo et al. Addition of the teaching of Unger to the combination does not remedy the deficit.

The Examiner states at page 7 of the Office Action, that the Unger et al., reference “is combined for its teachings of sterilization, Nyberg et al. teaches the preparation of phospholipids using instant steps a to c.” As set forth above, Nyberg et al. teaches the separation of combined lipids and fails to teach or suggest any process that includes steps a to c of the invention as claimed, which is the preparation of a uniform blend of phospholipids from separate, individual,

purified, phospholipids. As argued above, the combination of the teaching of Kissel et al., Kikuchi et al., Papahadjopoulos et al., and Lenk et al. with that of Nyberg et al. in view of Swaerd-Nordmo et al. fail to remedy the omission. The addition of the teaching of Unger et al. to the combination of the references still fails to teach or suggest each element of the claimed invention and a *prima facie* case for obviousness has not been established.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 115-116 under 35 U.S.C. §103(a) as unpatentable over Nyberg in view of Kissel or Papahadjopoulos or Lenk or Kikuchi, individually or in combination, in view of Swaerd-Nordmo, further in view of Unger.

The Examiner rejected claim 117 under 35 U.S.C. §103(a) as being unpatentable over Nyberg (5,677,472) in view of Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination, further in view of Unger 6,416,740. Applicant respectfully traverses the rejection.

Rejected claim 117 ultimately depends from claim 87. As discussed above, all elements of claim 87, as amended, are not taught or suggested by the combination of Nyberg et al., in view of Kissel et al., Kikuchi et al., Papahadjopoulos et al., and Lenk et al. Addition of the teaching of Unger to the combination does not remedy the deficit.

The Examiner states at page 8 of the Office Action, that the Unger et al., reference “is combined for its teachings of art known use of the claimed combination of the phospholipids; Nyberg et al. teaches the preparation of phospholipids using instant steps a to c.” As argued above, Nyberg et al. teaches the separation of combined lipids and fails to teach or suggest any process that includes steps a to c of the invention as claimed, which results in preparation of a uniform blend of phospholipids. As argued above, the combination of the teaching of Kissel et al., Kikuchi et al., Papahadjopoulos et al., and Lenk et al. with that of Nyberg et al. fail to remedy the deficit. The addition of the teaching of Unger et al. to the combination of the remaining references still fails to teach or suggest each element of claim 87, from which claim 117 ultimately depends, resulting in a failure to support a *prima facie* case for obviousness.

Accordingly, Applicant requests reconsideration and withdrawal of the rejection of claim 117 under 35 U.S.C. §103(a) as unpatentable over Nyberg in view of Kissel or Papahadjopoulos or Lenk or Kikuchi, individually or in combination, further in view of Unger.

The Examiner rejected claims 87-111 under 35 U.S.C. §103(a) as being unpatentable over Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination. Applicant respectfully traverses the rejection.

The Examiner at page 9 of the Office Action states “in essence” the Kissel et al., Papahadjopoulos et al., Lenk et al., or Kikuchi et al. references “teach steps d and e of claim 87.” The Examiner then concludes that “instant steps a-c in claim 87 just recite re-precipitation of the lipids used in the formation of lipid suspension.” Applicant respectfully disagrees with the Examiner’s conclusion. Steps (a)-(c) of claim 87 are based on the surprising discovery by the inventors that steps a-c are critical to obtaining uniformity in the size of the particles of the lipid suspension made from the lipid blend, and thus are necessary steps in the process as claimed.

The specification as filed teaches the novel steps of combining two or more isolated phospholipids together in a first non-aqueous solvent in which they dissolve and contacting the combined phospholipids with a second non-aqueous solvent that precipitates out both of the blended phospholipids. This permits one skilled in the art to prepare a uniform lipid blend that results in enhanced characteristics of the prepared lipid suspension, characteristics that differ from lipid suspensions prepared without steps a-c as claimed. The lipid suspension resulting from the claimed process is a more uniform suspension and has a uniform particle size. The combined teaching in the cited references and the knowledge in the art at the time of filing would have not provided one skilled in the art with any reason or motivation to perform the additional dissolution and precipitation steps (a-c) to make a lipid blend as part of a process to make a lipid suspension. In fact, it would not have been reasonable for one skilled in the art to include steps a-c as purification steps when preparing a lipid suspension from purified phospholipids. Including such a purification process would have been expected by one skilled in the art to result in a reduced yield – which would have been undesirable. The inclusion of steps a-c are critical in the invention as claimed because applicants understood that steps a-c were not purification steps, but rather served to increase the uniformity and particle size uniformity of the resulting

phospholipid suspension. This benefit would not have been recognized or understood by one of ordinary skill in the art based on the teaching of the Kissel et al., Papahadjopoulos et al., Lenk et al., or Kikuchi et al. references, or based on knowledge in the art at the time of filing.

The Kissel et al., Papahadjopoulos et al., Lenk et al., and Kikuchi et al. references all fail to teach or suggestion the steps a to c of claim 87 as claimed. Steps a to c are critical to the invention as claimed for making a uniform blend of phospholipids. The inclusion of steps a-c yields the unexpected result of a lipid suspension that has improved uniformity and more uniform particles. Knowledge in the art regarding the use of precipitation steps to remove impurities would not suggest to one of ordinary skill to use contact with multiple, additional non-aqueous solvents to remove impurities. The teachings of Kissel et al., Papahadjopoulos et al., Lenk et al., or Kikuchi et al. would not lead one to arrive at the instantly claimed invention – and the invention as claimed is not rendered obvious by the combined or individual cited references. Accordingly, Applicant requests reconsideration and withdrawal of the rejection of claims 87-111 under 35 U.S.C. §103(a) as being unpatentable over Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination. Applicant respectfully traverses the rejection.

The Examiner rejected claim 117 under 35 U.S.C. §103(a) as being unpatentable over Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination as set forth above, further in view of Unger 6,416,740. Applicant respectfully traverses the rejection.

Rejected claim 117 ultimately depends from claim 87. As discussed above, all elements of claim 87, as amended, are not taught or suggested by the combination of teachings of, or individual teaching provided by, Kissel et al., Kikuchi et al., Papahadjopoulos et al., or Lenk et al. Addition of the teaching of Unger to the combination does not remedy the deficit.

The Examiner states at page 10 of the Office Action that the Unger et al., reference “is combined for its teachings of art known use of the claimed combination of the phospholipids.” Applicant submits that, as argued above, Kissel et al., Kikuchi et al., Papahadjopoulos et al., and/or Lenk et al., alone and in combination, fail to teach or suggest any process that includes steps a to c of the invention as claimed. Steps a-c are critical steps in the claimed process.

Combining two or more individual purified lipids with non-aqueous solvents to prepare a lipid blend, dissolving that blend in a non-aqueous solution, and mixing the dissolved blend into an aqueous solution, are not taught or suggested by Kissel et al., Kikuchi et al., Papahadjopoulos et al., or Lenk et al. The lack of teaching or suggestion of elements of the invention as claimed supports a conclusion of non-obviousness over the cited art. The addition of the teaching of Unger et al. to the teaching of the individual Kissel et al., Kikuchi et al., Papahadjopoulos et al., or Lenk et al references, of any combination thereof, also fails to teach or suggest each element of the claimed invention and fails to support a *prima facie* case for obviousness.

Accordingly, Applicant requests reconsideration and withdrawal of the rejection of claim 117 under 35 U.S.C. §103(a) as unpatentable over Kissel or Papahadjopoulos or Lenk or Kikuchi, individually or in combination, further in view of Unger.

The Examiner rejected claims 87-111 and 117 under 35 U.S.C. §103(a) as being unpatentable over Munechika (5, 662,931) in combination with Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination. Applicant respectfully traverses the rejection.

The Examiner states at page 11 of the Office Action that Munechika discloses a method of preparing liposomes that includes “dissolving the lipids in an organic solvent, precipitating the lipids using a second organic solvent and hydrating the precipitate with an aqueous solution to form liposomes (col. 2, line 8 through col. 3, line 61 and examples). Applicant disagrees with the Examiner’s characterization of the Munechika et al. disclosure. Munechika describes making an emulsion that includes dissolving a lipid in a first organic solvent that is immiscible in water – followed by adding a “drug-containing aqueous solution” to the dissolved lipid and forming an emulsion (see abstract and col. 2, lines 63 to col. 3 line 2.) Munechika et al. teaches placing a drug into an aqueous solvent and adding that aqueous mixture to the first organic solvent that is immiscible in water. Munechika goes on to describe how the organic/aqueous emulsion can then be added to a second organic solvent, etc. Thus, the Examiner’s interpretation of the process taught by Munechika et al., is not accurate and omits Munechika’s step of adding an aqueous solvent to the first organic solvent in which water is immiscible. This clearly differs from, and is not suggestive of, the instantly claimed process.

One skilled in the art could not combine the disclosure of Munechika with that of Kissel et al., Kikuchi et al., Papahadjopoulos et al., and/or Lenk et al. to arrive at the instantly claimed invention. Rather, such a combination would include addition of an aqueous solvent to a lipid after the lipid had only been contacted with a single organic solvent that is immiscible in water. Thus, the disclosure of Munechika in effect, teaches away from the process of the instant claims and the combined teaching of Munechika et al. and that of Kissel et al., Kikuchi et al., Papahadjopoulos et al., and/or Lenk et al. and would not result in the invention as claimed.

Accordingly, Applicant requests reconsideration and withdrawal of the rejection of claims 87-111 and 117 under 35 U.S.C. §103(a) as unpatentable over Munechika in combination with Kissel or Papahadjopoulos or Lenk or Kikuchi, individually or in combination.

The Examiner rejected claims 112-114 under 35 U.S.C. §103(a) as being unpatentable over Munechika (5,662,931) in combination with Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination in view of Swaerd-Nordmo (6,165,442). Applicant respectfully traverses the rejection.

Rejected claims 112-114 ultimately depend from claim 87. As discussed above, all elements of claim 87, as amended, are not taught or suggested by the combination of Munechika et al., in view of Kissel et al., Papahadjopoulos et al., Lenk et al., or Kikuchi et al. The addition of the teaching of Swaerd-Nordmo et al. to the combination does not remedy the deficit.

The Examiner indicates at page 12 of the Office Action, that the Swaerd-Nordmo reference teaches “exchanging perfluoropropane in a vacuum chamber.” As set forth above, Munechika et al. teaches a process with steps of contacting a lipid with an organic solvent that is immiscible in water, then contacting the mixture with an aqueous solvent/drug solution to form an emulsion. This teaching differs substantially from the instantly claimed invention and fails to teach or suggest any process that includes steps a to c of the invention as claimed, which results in a uniform blend of phospholipids. As argued above, the combination of the teaching of Kissel et al., Papahadjopoulos et al., Lenk et al., and/or Kikuchi et al., with that of Munechika et al. fails to remedy the omission. The addition of the teaching of Swaerd-Nordmo et al. to the combination of the references does not teach or suggest each element of the claimed invention and a *prima facie* case for obviousness has not been established.

Accordingly, Applicant requests reconsideration and withdrawal of the rejection of claims 112-114 under 35 U.S.C. §103(a) as unpatentable over Munechika in combination with Kissel or Papahadjopoulos or Lenk or Kikuchi, individually or in combination in view of Swaerd-Nordmo (6,165,442).

The Examiner rejected claims 115-116 under 35 U.S.C. §103(a) as unpatentable over Munechika (5,662,931) in combination with Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination in view of Swaerd-Nordmo (6,165,442) as set forth above, further in view of Unger (6,416,740). Applicant respectfully traverses the rejection.

Rejected claims 115-116 ultimately depend from claim 87. As discussed above, all elements of claim 87, as amended, are not taught or suggested by the combination of Munechika et al., in combination with Kissel et al., Papahadjopoulos et al., Lenk et al., or Kikuchi et al., and in view of Swaerd-Nordmo et al. The addition of the teaching of Unger et al., to the combination does not remedy the deficit.

The Examiner indicates at page 13 of the Office Action, that the Unger et al. reference teaches “final sterilization of the product.” Applicant submits that, as argued above, Munechika et al. teaches a process that, in part, includes steps of contacting a lipid with an organic solvent that is immiscible in water, then contacting the mixture with an aqueous solvent/drug solution to form an emulsion. This teaching differs substantially from the instantly claimed invention set forth and fails to teach or suggest any process that includes steps a to c of the invention as claimed, which results in a uniform blend of phospholipids. As argued above, the combination of the teaching of Kissel et al., Papahadjopoulos et al., Lenk et al., and/or Kikuchi et al., and Swaerd-Nordmo et al. with that of Munechika et al. fails to remedy the omission. The addition of the teaching of Unger et al. to the combination of the references also does not result in a combination that teaches or suggests each element of the claimed invention. A *prima facie* case for obviousness is not supported.

Accordingly, Applicant requests reconsideration and withdrawal of the rejection of claims 115-116 under 35 U.S.C. §103(a) as unpatentable over Munechika in combination with

Kissel or Papahadjopoulos or Lenk or Kikuchi, individually or in combination in view of Swaerd-Nordmo, as set forth above, further in view of Unger.

The Examiner rejected claim 117 under 35 U.S.C. §103(a) as being unpatentable over Munechika (5,662,931) in combination with Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination as set forth above, further in view of Unger 6,416,740. Applicant respectfully traverses the rejection.

Rejected claim 117 ultimately depends from claim 87. As discussed above, all elements of claim 87, as amended, are not taught or suggested by the teaching of Munechika et al. in combination with Kissel et al., or Papahadjopoulos et al., or Lenk et al., or Kikuchi et al. The addition of the teaching of Unger et al., to the combination does not remedy the deficit.

The Examiner indicates at page 13-14 of the Office Action, that the Unger et al. reference teaches use of a combination of DPPA, DPPE-PEG5000 and DPPC in liposome preparation. The Unger et al. reference, however, does not teach the preparation of a phospholipid blend using instant steps a to c. Applicant submits that, as argued above, Munechika et al. teaches a process that, in part, includes steps of contacting a lipid with an organic solvent that is immiscible in water, then contacting the mixture with an aqueous solvent/drug solution to form an emulsion. This teaching differs substantially from the instantly claimed invention set forth and fails to teach or suggest any process that includes steps a to c of the invention as claimed, which results in a uniform blend of phospholipids. As argued above, the combination of the teaching of Munechika et al. with that of Kissel et al. or Papahadjopoulos et al. or Lenk et al., or Kikuchi et al., fails to remedy the omission. The addition of the teaching of Unger et al. to the combination of the references does not result in a combination that teaches or suggests each element of the claimed invention. *A prima facie* case for obviousness has not been established.

Accordingly, Applicant requests reconsideration and withdrawal of the rejection of claim 117 under 35 U.S.C. §103(a) as unpatentable over Munechika in combination with Kissel or Papahadjopoulos or Lenk or Kikuchi, individually or in combination as set forth above, further in view of Unger 6,416,740.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. N0469.70022US02.

Respectfully submitted,

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